

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 14160-2PCT		Date of mailing (day/month/year) 18 APR 2006
		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US04/37587	International filing date (day/month/year) 13 November 2004 (13.11.2004)	Priority date (day/month/year) 14 November 2003 (14.11.2003)
International Patent Classification (IPC) or both national classification and IPC IPC(8): C07H 21/04 and US Cl.: 536/23.1		
Applicant BIOVENTURES, INC.		

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

+ $\frac{11-14-03}{22}$
9-14-05

$\frac{4-18-06}{3mo}$
7-18-06

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Date of completion of this opinion 22 March 2006 (22.03.2006)	Authorized officer Jehanne S. Sitton Telephone No. 571-272-0500
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Form PCT/ISA/237 (cover sheet) (April 2005)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/37587

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☒ on paper
☒ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
☐ filed together with the international application in electronic form.
☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37587

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-11</u>	YES
	Claims <u>none</u>	NO
Inventive step (IS)	Claims <u>1-11</u>	YES
	Claims <u>none</u>	NO
Industrial applicability (IA)	Claims <u>1-11</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-11 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest genetic material comprising any of haplotypes 8-10, or isolated genetic material comprising the indicated microsatellite markers in combination, or genetic material comprising the indicated haplotypes in combination with either a nucleic acid molecule comprising at least 17 consecutive nucleotides of SEQ ID NO: 1 with the variations indicated in claim 2(b), or any of the haplotypes listed in claim 2(c). Further, the art does not teach or suggest a method of diagnosing dyslexia with any of the isolated genetic material as set forth in claims 1 or 2, or a method of classifying a dyslexic individual by diagnosing dyslexia or a predisposition to dyslexia using any of the isolated genetic material as set forth in claims 1 or 2. Additionally, the prior art does not teach or suggest a method of ameliorating the symptoms of dyslexia by diagnosing dyslexia or a predisposition to dyslexia in an individual using any of the isolated genetic material as set forth in claims 1 or 2 and treating the individual.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1 and 2 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 1 and 2 are indefinite for the following reason(s): It is unclear from the claimed recitation as to whether the genetic material encompassed by the claims includes one nucleic acid molecule or multiple molecules. For example, in claim 1 it is unclear if the molecule comprises the full region in between the microsatellite markers as well as SEQ ID NO: 1, or separate molecules comprising portions of the regions. Additionally, it is unclear whether in claim 2, the claim further limits the specific molecule of claim 1, or is drawn to added molecules each possibly comprising a different haplotype, or portions of such on separate molecules.

Claim 3-11 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The application, as originally filed, did not describe: methods of diagnosis or ameliorating the symptoms of dyslexia or preventing dyslexia. The claims encompass diagnosis based on the detection of one of haplotypes 8-10, however as noted in the application, the results of analysis for the 190,198, 214,190 and 214,192 microsatellite combination were only 3.2 to 9.5, 1.6 to 2 or 1.2 to 3.6, respectively, fold greater for dyslexics than non dyslexics. The application concludes that these can be used to determine risk of occurrence, not diagnosis. Further, at page 23, the application teaches haplotypes 5-11 occurred in only the dyslexic population, however the claims encompass diagnosis with other haplotypes. The application concludes that these haplotypes are associated with the risk of exhibiting dyslexic phenotypes, but does not teach that one can diagnose an individual based on such haplotypes. The application is further unclear in that it cannot be determined whether the haplotypes 5-11 at line 35 correspond to the haplotypes in table 5, or how they correlate to the haplotypes in table 5. The application provides no teaching of treatment of dyslexia such as amelioration of symptoms or prevention of dyslexia.

Claims 3-11 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: The claims encompass diagnosis based on the detection of one of haplotypes 8-10, however as noted in the application, the results of analysis for the 190,198, 214,190 and 214,192 microsatellite combination were only 3.2 to 9.5, 1.6 to 2 or 1.2 to 3.6, respectively, fold greater for dyslexics than non dyslexics. The application concludes that these can be used to determine risk of occurrence, not diagnosis. Given that for some markers, the values were not much greater than 1 for dyslexics than non-dyslexics, the use of the markers to diagnose dyslexia is not predictable. Further, at page 23, the application teaches haplotypes 5-11 occurred in only the dyslexic population, however the claims encompass diagnosis with other haplotypes. The application concludes that these haplotypes are associated with the risk of exhibiting dyslexic phenotypes, but does not teach that one can diagnose an individual based on such haplotypes. The application is further unclear in that it cannot be determined whether the haplotypes 5-11 at line 35 correspond to the haplotypes in table 5, or how they correlate to the haplotypes in table 5. The application does not provide any statistical values to assess the predictability of the results disclosed. The application provides no teaching of treatment of dyslexia such as amelioration of symptoms or prevention of dyslexia.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.